Patent claims:

1. Method for modulating regulatory RNA-ligand interactions comprising
(a) defining and selecting a secondary structure element of an RNA molecule which is required for the recognition by a ligand, e.g. protein,
(b) calculating the thermodynamic probability of the secondary structure element of step a) in the secondary structure ensemble of said RNA,
(c) calculating the thermodynamic probability of the secondary structure element of step a) in the secondary structure ensemble of said RNA hybridized to an at least partly reverse complementary oligonucleotide,
(d) determining an oligonucleotide that changes the thermodynamic probability of said secondary structure element beyond a defined probability threshold,
(e) providing an oligonucleotide as determined in step (d), and optionally,
(f) hybridizing an RNA comprising said secondary structure element of step (a) to an oligonucleotide of step (e), and
(g) determining the effect of said hybridization on the thermodynamic probability of said secondary structure element.

2. Method of claim 1, wherein the RNA is an IL-2 mRNA, the ligand is ELAVL1 and the oligonucleotide has a sequence selected from the group consisting of
SEQ ID NO 1: AAGGCCTGATATGTTTTAAG,
SEQ ID NO 2: AATATAAAATTTAAATATTT,
SEQ ID NO 3: TAGAGCCCCTAGGGCTTACA,
SEQ ID NO 4: TGAAACCATTTTAGAGCCCC,
SEQ ID NO 5: AAGGCCUGAUAUGUUUUAAG,
SEQ ID NO 6: AAUAUAAAAUUUAAAUAUUU,
SEQ ID NO 7: UAGAGCCCCUAGGGCUUACA,
SEQ ID NO 8: UGAAACCAUUUUAGAGCCCC.

3. Method of claim 1, wherein the RNA is a TNF-α mRNA, the ligand is ELAVL1 and the oligonucleotide has a sequence selected from the group consisting of
SEQ ID NO 9: TCGGCCAGCTCCACGTCCCG,
SEQ ID NO 10: TCTGGTAGGAGACGGCGATG,
SEQ ID NO 11: ACGGCGATGCGGCTGATGGT,

SEQ ID NO 12: TTCTGGAGGCCCCAGTTTGA,
SEQ ID NO 13: ATTCCAGATGTCAGGGATCA, and
SEQ ID NO 14: ATCACAAGTGCAAACATAAA,

4. Use of a method of any one of claims 1 to 3 for manipulating the expression of a gene by altering the secondary structure of the corresponding RNA.

5. Assay for identifying an agent that modulates the effect of the hybridization of an RNA molecule to an oligonucleotide comprising
(a) hybridizing an RNA comprising a secondary structure element which is required for recognition by a ligand to an oligonucleotide that changes the thermodynamic probability of said secondary structure element beyond a defined probability threshold in the presence and in the absence of a candidate compound,
(b) determining the effect of hybridization of said RNA to said oligonucleotide in the presence and in the absence of said candidate compound,
(c) identifying an agent which modulates the effect of hybridization.

6. Assay for identifying an agent that mimics the effect of hybridization of an RNA molecule to an oligonucleotide comprising
(a) hybridizing an RNA comprising a secondary structure element which is required for recognition by a ligand to an oligonucleotide that changes the thermodynamic probability of said secondary structure element beyond a defined probability threshold
(b) hybridizing an RNA comprising a secondary structure element which is required for recognition by a ligand to a candidate compound which is expected to have a similar effect as the oligonucleotide,
(c) determining the effect of hybridization for steps (a) and (b), and
(d) identifying an agent which mimics the effect of hybridization of step (a).

7. Assay of any one of claims 5 or 6, wherein the effect of hybridization is determined by measuring a signal which is related to the effect of hybridization, which effect is selected from the group consisting of changes in secondary RNA structure, tertiary RNA structure, RNA-ligand affinity, RNA oligo- or multimerization, ligand oligo- or multimerization, conformational change of the ligand, efficiency of a downstream effect of RNA-ligand recognition, RNA splicing, covalent RNA modifications, RNA localization, RNA stability,

RNA translation and protein expression profiles.

8. Assay of any one of claims 5 to 7 wherein the RNA is an mRNA.

9. Assay of any one of claims 5 to 8, wherein the RNA, the ligand and the oligonucleotide are as defined in claim 2 or 3.

10. Use of an assay of any of claims 5 to 9 for high throughput screening.

11. Agent identified by an assay of any one of claims 5 to 9 for use as a pharmaceutical.

12. An oligonucleotide that changes the thermodynamic probability of a secondary structure element beyond a defined probability threshold identified by a method of claim 1.

13. An oligonucleotide of claim 12 having a sequence selected from the group consisting of

SEQ ID NO 1: AAGGCCTGATATGTTTTAAG,
SEQ ID NO 2: AATATAAAATTTAAATATTT,
SEQ ID NO 3: TAGAGCCCCTAGGGCTTACA,
SEQ ID NO 4: TGAAACCATTTTAGAGCCCC,
SEQ ID NO 5: AAGGCCUGAUAUGUUUUAAG,
SEQ ID NO 6: AAUAUAAAAUUUAAAUAUUU,
SEQ ID NO 7: UAGAGCCCCUAGGGCUUACA,
SEQ ID NO 8: UGAAACCAUUUUAGAGCCCC.
SEQ ID NO 9: TCGGCCAGCTCCACGTCCCG,
SEQ ID NO 10: TCTGGTAGGAGACGGCGATG,
SEQ ID NO 11: ACGGCGATGCGGCTGATGGT,
SEQ ID No 12: TTCTGGAGGCCCCAGTTTGA,
SEQ ID NO 13: ATTCCAGATGTCAGGGATCA, and
SEQ ID NO 14: ATCACAAGTGCAAACATAAA,

14. An oligonucleotide identified by a method of claim 1 or an oligonucleotide of claim 13, in which the oligonucleotide is an RNA or DNA molecule with any chemical modification.

15. An oligonucleotide identified by a method of claim 1 or an oligonucleotide of claim 13, in which the oligonucleotide is a peptoid nucleic acid or a locked nucleic acids molecule

16. Use of an oligonucleotide of any one of claims 12 to15 for manipulating regulatory RNA-ligand interactions.

17. Use of an oligonucleotide of any one of claims 12 to 15 for influencing the stability of an RNA molecule.

18. Pharmaceutical composition comprising an agent identified by an assay of claim 5 or an oligonucleotide of any one of claims 12 to 15 beside at least one pharmaceutical excipient.

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